Modeling Brain Adaptation to Focal Damage

Sharon Goodall*, James A. Reggia*+, and Sungzoon Cho°
Depts of Computer Science* & Neurology+, Univ. of Maryland College Park, MD 20742
° Dept of Computer Science & Engr., Pohang Inst of Science & Technology, Pohang, Kyungbook 790-784, Korea

Determining how feature maps in the cerebral cortex adapt to sudden, focal damage is important for gaining a deeper understanding of neurological illnesses such as stroke. In this paper we describe a neural model of the region of primary sensory cortex related to upper extremity proprioception, and show how the feature map there reorganizes following a simulated lesion. A perilesion zone with decreased activity appears and then gradually expands with time. These results differ from those seen with previous models of cortical lesions, and offer an alternative mechanism to the "ischemic penumbra" seen in certain types of stroke.

INTRODUCTION

As neural modeling technology has matured during the last several years there has been an increasing interest in adopting neural models to simulate disorders in neurology, neuropsychology, and psychiatry. For example, models of memory loss in dementia, epilepsy, aphasia, dyslexia, and schizophrenia have been studied to obtain a better understanding of the underlying pathophysiological processes. A recent review summarizes this rapidly growing area of research [8].

Many past computational models of the cerebral cortex have concentrated on map formation since this is a prevalent organizational structure in the mammalian brain[9]. A *cortical map* refers to a representation of the body surface or external world over the two-dimensional surface of the cerebral cortex. Cortical maps preserve a similarity relationship for input patterns, and can be divided into two classes. For *topographic* maps, similarity of input patterns is measured in terms of their geometric proximity; they occur, for example, in mammalian somatosensory cortex. For *feature* maps, the similarity measure can represent any functional correspondence of the input patterns. The well-known map of orientation-specificity in visual cortex provides an example. While computational models of topographic map formation have been studied previously [5, 7], there has been very little work on cortical lesioning with this class of maps. Feature maps, which generalize the concept of topographic maps, have also been modeled [4, 6, 9] but to date no cortical lesioning studies have been done with this type of map to our knowledge.

In this paper we describe the use of a neural model to simulate adaptation of the cerebral cortex to a sudden focal lesion such as occurs in stroke. Stroke is a major health problem in the United States: it has long been the third leading cause of death, and it carries an annual economic cost of over $13 billion [1, 3]. In spite of this and the complex, incompletely understood pathophysiological processes involved, very little past work has been done to develop a computational model of stroke. In fact, the one previous study that attempted to model a small cortical lesion was not successful in producing the spontaneous reorganization seen in experimental animal studies [5]. Only during the past year was a neural model of cortex that spontaneously reorganizes following an acute focal lesion first reported [2, 10]. When a small lesion was introduced into the cortical representation of the sensory surface of the hand, the model cortex reorganized so that the hand surface originally represented by the lesioned area spontaneously reappeared in adjacent cortical areas, as has been seen experimentally. Both of these studies applied lesions to topographic maps only.

Recently, we developed a model of cortical feature map formation based on proprioceptive input from a simulated upper extremity [4]. Proprioceptive cortex receives sensory information from muscles, tendons and joints enabling the nervous system to determine extremity position and movement. In this paper we focus on sensory information about muscle length and tension. In contrast to the maps used in previous lesioning studies of model cortex, this map is not a topographic rep-

0195-4210/94/$5.00

resentation of skin surface but is a feature map of individual sensory features (e.g., individual muscle lengths and tensions). Surprisingly, the pattern of reorganization observed was quite different from that seen with previous lesion simulations of a topographic map [2, 10]. A region of decreased activity surrounding the lesion developed and then gradually expanded. In the following, we describe this result, offer an explanation for why it occurs, and describe how it may relate to recent empirical observations made in animal models of stroke.

METHODS

We briefly review our model of proprioceptive map formation [4], and then describe how it is lesioned.

Model Arm

Fig. 1 shows the structure of the neural model of the proprioceptive cortex. Inputs to the arm layer are calculated from a simulated model arm. This model arm is a great simplification of biological reality, and is intended as only a first effort for modeling feature map formation in the motor and somatosensory cortex [4]. It consists of upper and lower arm segments, connected at the elbow. It has only six generic muscles or muscle groups, each of which corresponds to multiple muscles in a real arm. We assume that there are four muscles that control the upper arm and two muscles that control the lower arm. Abductor and adductor muscles move the upper arm up and down through 180°, respectively, while flexor and extensor muscles move it forward and backward through 180°, respectively. The lower arm flexes and extends as much as 180° in a plane, controlled by lower arm flexor and extensor muscles. When the model arm is placed into a specific spatial position, it generates input signals to the cortex from the sensory neurons ("arm layer" in Fig. 1) that indicate individual muscle lengths and tensions. The biologically-oriented input to our model, based on muscle stretch and tension, distinguishes it from several previous robotically-oriented neural models of arm control where input is typically derived from a camera (e.g., [9]). Further details on the model arm can be found in [4].

Neural Computations

The model neural network has two separate layers of units (Fig. 1), an arm layer and a proprioceptive cortex layer. The arm layer consists of

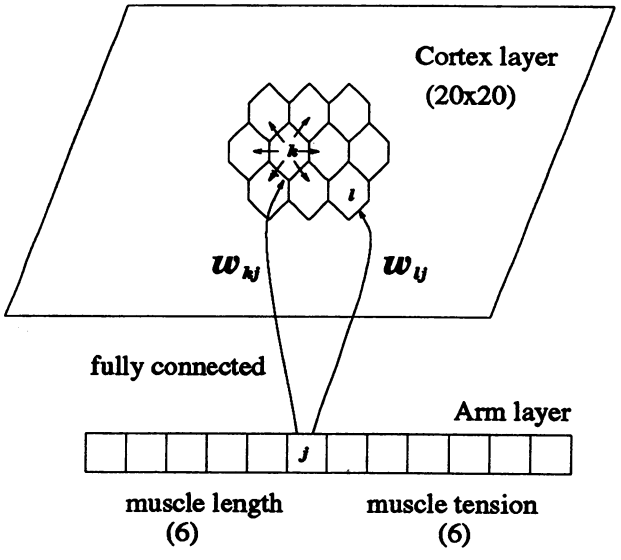

Figure 1: Structure of Neural Network Model

12 units which represent six muscle length and six muscle tension measures. A length unit becomes active when the corresponding muscle is stretched, while a tension unit becomes active when the corresponding muscle produces tension through active contraction. Each unit in the arm layer competitively distributes its activation to every unit in the cortex layer. The connection weights were trained starting from an initial random uniform distribution. The proprioceptive cortex layer consists of a grid of 20 × 20 units. Each unit represents a cortical column, and is connected to its six immediate neighboring units in a hexagonal tessellation. To remove edge effects, units on the edges of the cortical sheet are connected with units on the opposite edges forming a torus.

A competitive activation mechanism is used to control the spread of activation [4]. One distinct feature of a competitive activation mechanism is its ability to induce lateral inhibition among units, and thus to support map formation, without using explicit inhibitory connections. The activation level of unit k at time t, $a_k(t)$ is determined by

$$\frac{da_k(t)}{dt} = c_s a_k(t) + (max - a_k(t)) in_k(t) \qquad (1)$$

where

$$in_k(t) = \sum_j c_p \frac{(a_k(t)+q)w_{kj}}{\sum_l (a_l(t)+q)w_{lj}} a_j(t). \qquad (2)$$

Here $c_s < 0, c_p > 0, max > 0$ and $q > 0$ are constants. The weight of the connection from unit j to unit k is denoted by w_{kj}, which is assumed

to be zero if there is no connection between the two units, as is the case with some intracortical connections. Weights are a function of time, but activation levels change much faster than weights. The output from unit j to unit k is proportional not only to the sender's activation level $a_j(t)$, but also to the receiver's activation level, $a_k(t)$.

Connection weights are modified according to competitive learning, a variant of Hebbian Learning that tends to change the incoming weight vectors of the output units (cortical layer units) into prototypes of the input patterns. Only the 4800 weights from the arm layer to the cortex layer change and this occurs through the learning rule $\Delta w_{kj} = \eta[a_j - w_{kj}]a_k^*$, where $a_k^* = a_k - \theta$ if $a_k > \theta$; and 0 otherwise (η is a small learning constant). The value θ is fixed throughout training.

Map Formation

A version of the neural model described above was trained as follows. Random input signals to the muscles were simulated as inputs to the model arm. These inputs specified positions of the model arm in 3-D space. From these model arm input values, arm layer muscle length and tension inputs were calculated. One thousand random input patterns, covering the input space, were presented to the network during training, after which further training did not produce qualitative changes in the trained weights. The neural model parameters were set empirically as follows. For cortical units, decay constant c_s and ceiling max in Eq. 1 were set to -4.0 and 5.0 respectively. Their q and output gain parameter c_p values in Eq. 2 were set to 0.001 and 0.9, respectively. For arm layer units, q and c_p values in Eq. 2 were set to 0.1 and 0.8, respectively. The learning rate η and θ value in the learning rule were empirically set to 0.1 and 0.32, respectively.

The trained network produced several results. Muscle length and tension maps formed during training. To examine the formation of muscle length and tension maps, the network was analyzed to determine which muscle length and tension input each cortical unit responded most strongly. Twelve input patterns were presented, each having only one muscle length or tension unit (arm unit) activated. Since the arm units represent the length and tension of the six muscles of the model arm, each test pattern corresponded to the unphysiological situation where either the length or tension of only one muscle is activated

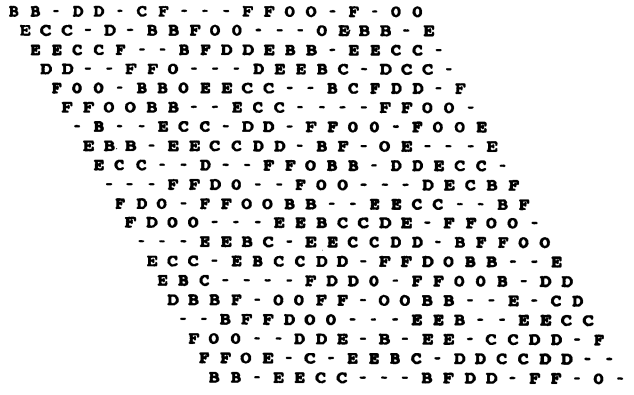

Figure 2: Cortical units tuned to muscle length after training.

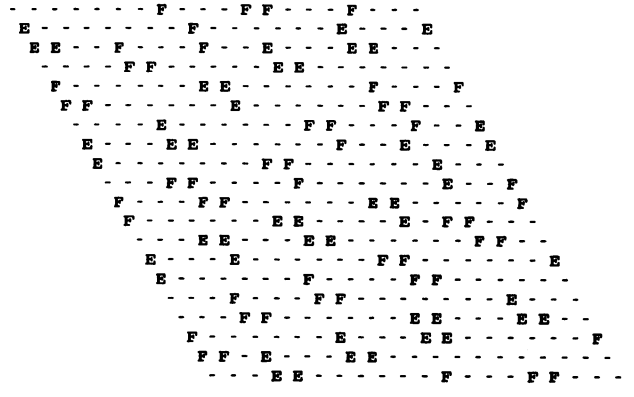

Figure 3: Cortical units trained to upper arm extensor (E) and flexor (F) muscle lengths after training.

(this was *not* the case with the training patterns). A cortical unit is taken to be "maximally tuned" to an arm input unit if the activation corresponding to the input unit is largest and above a threshold of 0.5.

Fig. 2 shows the maximal tuning of cortical units to muscle length after training. The muscle lengths are labeled as follows: E for upper arm extensor, F for upper arm flexor, B for upper arm abductor, D for upper arm adductor, O for lower arm extensor and C for lower arm flexor (e.g., the unit in the upper left corner of the cortex is maximally tuned to the upper arm abductor (B) for muscle length). Cortex units marked "-" were found not to be tuned to the length of any muscle. Clusters of units responsive to the same muscle became more uniform in size after training. The size of the clusters ranged from 2 to 10 before training, but ranged from 3 to 4 after training, and their shape became more regular.

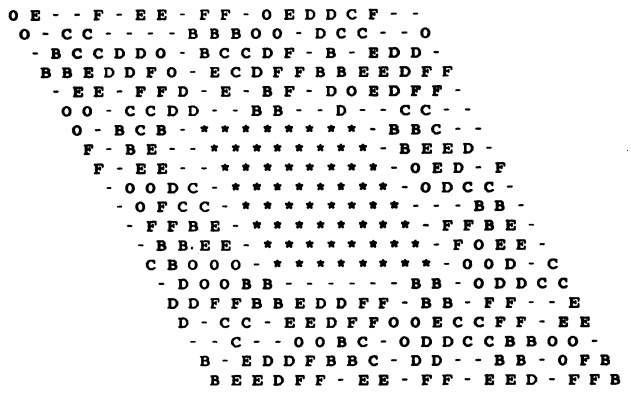

Figure 4: Muscle length tuning of cortex layer after lesion.

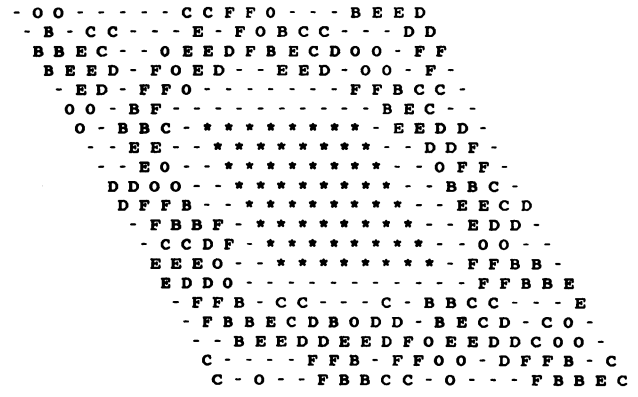

Figure 5: Muscle length tuning of cortex layer after further training.

Although difficult to see in Fig. 2, clusters of units tuned to antagonist muscles were usually pushed maximally apart from one another during training. Consider the clusters shown in Fig. 3, where only those units tuned in Fig. 2 to upper arm extensor (E) and flexor muscles (F) are displayed. After training, the clusters of "E"s and "F"s are generally pushed maximally apart, evenly spaced and more uniform in size. The network thus captures the mechanical constraint imposed by the model arm that two antagonist muscles cannot be stretched at the same time.

Lesioning the Model

For this study, an 8 by 8 contiguous patch of the cortex layer in the trained network was lesioned to simulate a sudden focal lesion such as occurs in stroke. For lesioned cortical units, the activation of the unit was fixed at 0.0. In addition, connections to lesioned cortical units were severed. The effect of the lesion on map formation was examined immediately following the lesion and after continually training the network with 4000 additional random patterns. A copy of the intact trained network before lesioning was also continually trained with the same 4000 random patterns to serve as a control. Little change was seen in the feature map with the control network.

RESULTS

Our study of simulated lesions in a proprioceptive cortical map has produced strikingly different results from those found with topographic maps [2, 5]. For example, Fig. 4 shows the muscle length map of the cortex layer immediately following the focal lesion. The lesion site is marked by "*"s. A perilesion zone of relatively inactive cortical elements ("-"s) appears. With time, as the map reorganizes in the context of continued proprioceptive input, the perilesion zone gradually expands, as is seen in Fig. 5 (after 4000 further random input stimuli). This perilesion zone is due to loss of intracortical excitatory connections from the lesioned region to surrounding elements, and it expands due to synaptic changes of the competitive learning process. There is also dramatic reorganization of the rest of the map, with 68% of the remaining elements changing the muscle group to which they are most sensitive (compare Figs. 4 and 5). However, the rearrangement may not be as complete as the figures suggest, since the maps show maximal tuning of cortical units. With further learning, the perilesion zone enlarges slightly and reorganization of the map continues.

Further evidence of the dynamics of the perilesion zone of inactivity is provided through an analysis of the mean activation level of cortical units averaged over all the test input patterns. We examined the mean activation level of cortical units at various distances from the lesion site. Before the lesion was introduced, the mean activation level of all regions was 0.18. Immediately after the lesion, the mean activation of the cortical units directly adjacent to the lesion site (distance d=1) dropped to 0.04 and additional training of the lesioned network produced a further drop to 0.01. Cortical units at distance d=2 from the lesion experienced a slight increase in mean activation immediately following the lesion(0.20); further training produced a drop in mean activation to 0.09. Cortical units at a distance d=3 experi-

enced a significant jump in mean activation level to 0.32, which diminished somewhat with training (0.29), while those at distances greater than 3 experienced an increase after training (0.20 following the lesion, 0.27 after further training). For the cortical layer as a whole, the mean activation following the lesion was 0.21, even after training.

Most interesting are the results seen at a distance d=2 from the lesion site. These cortical units are responsive immediately following the lesion, suggesting that there is potential for preventing growth of the perilesion zone of impairment. However, after further training, they too become part of the inactive region, as evidenced by the decreased mean activation level for this zone after training. Immediately following the lesion, elements bordering the lesion channel a greater percentage of their output to cortical units at a distance d=2 from the lesion site. However, synaptic changes from further training reverse this effect, thereby extending the inactive perilesion zone.

CONCLUSIONS

A model of cortical map formation based on proprioceptive input from a simulated upper extremity was used to simulate brain adaptation to a sudden focal lesion such as transpires with stroke. A region of depressed activity surrounding the lesion site appeared immediately following introduction of a sudden focal lesion, and gradually increased in size with further training of the neural model. This result is strikingly different from that seen with model topographic maps [2, 10], and developing a better understanding of the different mechanisms involved is an important research priority. The inactive perilesion zone seen here is particularly interesting because it resembles the ischemic penumbra described in stroke, where neurons surrounding a brain infarction can be dysfunctional but not dead [3]. Our results suggest the hypothesis that in some situations part of the ischemic penumbra may be caused by a loss of lateral excitatory connections from the lesioned region, and this may worsen due to normal synaptic plasticity. This contrasts with the more generally held view that the dysfunctional lesion area is caused by borderline ischemia only.

This computational model of feature map adaptation to sudden focal damage is of interest to the modeling community as a whole as it demonstrates that current neural network models can be used effectively to study diseases. Neural models that simulate disorders compliment traditional methods for examining brain disorders. Lesion size and location can be controlled and uniformly varied over large numbers of hypothetical subjects. The simulations also permit detailed inspection of the mechanisms underlying brain disorders.

Acknowledgement: This work was supported by NINCDS awards NS 29414 and NS 16332.

References

[1]. AHA. *Stroke Facts*, AHA, Dallas, 1989.

[2]. Armentrout S, Reggia J and Weinrich M A. A Neural Model of Cortical Map Reorganization Following a Focal Lesion, *Artificial Intelligence in Medicine*, 1994, in press.

[3]. Caplan L. Stroke, Butterworth, 1993.

[4]. Cho S, and Reggia J. Map Formation in Proprioceptive Cortex. *Internat. J. of Neural Systems*, 1994, in press.

[5]. Grajski K, and Merzenich M. Hebb-Type Dynamics is Sufficient to Account for the Inverse Magnification Rule in Cortical Somatotopy, *Neural Computation*, 2, 1990, 71-84.

[6]. Miller K, Keller J, and Stryker M. Ocular Dominance Column Development, *Science*, 245, 1989, 605-615.

[7]. Pearson J, Finkel L, and Edelman G. Plasticity in the Organization of Adult Cerebral Cortical Maps: A Computer Simulation Based on Neuronal Group Selection, *J of Neuroscience*, 7(12), 1987, 4209-4223.

[8]. Reggia J. Neural Computation in Medicine, *Artif. Intell. in Med.*, 5, 1993, 143-157.

[9]. Ritter H, Martinetz T, and Schulten K. *Neural Computation and Self-Organizing Maps*, Addison-Wesley, 1992.

[10]. Sutton G, Reggia J, Armentrout S, and D'Autrechy C. Map Reorganization as a Competitive Process, *Neural Computation*, 6, 1994, 1-13.